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Can pan-immune inflammation value and systemic inflammatory response index be used clinically to predict inflammation in patients with cataract?

Can inflammatory indexes clinically important in patients with cataract?

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Abstract
Aim: It is known that inflammatory processes increase the risk of cataract formation. There are no studies examining inflammatory indices in patients with cataract. Therefore, this is the first study that simultaneously investigates the systemic inflammatory response index (SIRI) and pan-immune-inflammation value (PIV) in patients with cataract.
Material and Methods: Ninety-five patients and 80 healthy controls who were examined at the Ophthalmology clinics of Aksaray University Education and Research Hospital between January 2022 and January 2023 were included in this retrospective study. The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), systemic immune-inflammation index (SII), SIRI and PIV values were calculated as indicators of the inflammatory process.
Results: The mean age of the patients was 68.3 ± 12.1 years and 54.7% of cataract patients were females. In the control group, the mean age was 66.5 ± 5.4 years, and 32.5% of the participants were females. There was no significant difference between the patient and control groups in terms of laboratory parameters ($p>0.05$). In addition, inflammatory indices were calculated for the patient and control groups. No statistically significant difference was found between NLR, PLR, LMR, SII, SIRI, and PIV between the groups ($p>0.05$).
Discussion: This study indicates that SIRI and PIV can be used in the evaluation of cataract patients. Therefore, Hemogram parameters and inflammatory indexes created with their combination may contribute to monitoring the progression of cataracts.

Keywords
Cataracts, Inflammation, Systemic Inflammatory Response Index, Pan-Immune-Inflammation Value

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Introduction

Cataract is the most common cause of visual impairment, affecting millions of people around the world, and its incidence is very high, especially in developing countries [1]. Age-related cataract is a common disease, the prevalence of which increases steeply past the age of 60 years. The prevalence of cataract was reported as 8-50% between the ages of 40-59, and 20-88% over the age of 60 [2]. There have been implicated risk factors including diabetes mellitus, inflammatory diseases, aging, genetic factors, drugs, smoking, malnutrition, and radiation in cataract formation [3]. Under normal conditions, oxidant and antioxidant molecules are in balance in our bodies [4-6].

As a result of the abnormal increase of free radicals, this balance is disrupted and causes oxidative stress (OS) and is accepted as one of the main underlying causes of cataract disorder [1, 7]. The accumulation of oxidized lens components as a result of the increase in reactive oxygen species (ROS) due to aging, the decrease in endogenous antioxidants, and the decrease in the efficiency of the mechanisms involved in their repair play an important role in the formation of cataracts [3].

Inflammation occurs after surgery and pathological injury, and can cause eye diseases leading to vision impairment [8]. It has been shown that ocular inflammation significantly increases the risk of cataract formation due to various factors or as a result of systemic inflammatory processes [9]. OS and Ocular inflammation (OI) are closely related pathophysiological processes, and both processes are simultaneously found in many pathological conditions, including age-related cataracts [10]. During the inflammatory process, activated phagocytic cells such as neutrophils and macrophages may play a role in cataract pathophysiology by producing large amounts of ROS [1]. In the literature, several studies have investigated the association between systemic inflammation and cataract, reporting associations between blood biomarkers including intracellular adhesion molecule-1, interleukin-6 (IL-6), transforming growth factor-beta (TGF-β), interferon-gamma (INF-γ), calprotectin [11-14]. In the studies, inflammatory indices such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and lymphocyte-to-monocyte ratio (LMR) have been reported as indicators of systemic and ocular inflammation [15]. It has been reported that a new inflammatory marker, Systemic immune-inflammation index (SII), is a prognostic indicator in various diseases such as primary open-angle glaucoma, dry eye disease, diabetic retinopathy, retinal vein occlusion and retinal artery occlusion [16-20]. Systemic inflammatory response index (SIRI) and pan-immune-inflammation value (PIV) are newly designed indexes that are considered comprehensive indicators of the immune response and systemic inflammation. The SIRI and PIV are important in the prognosis or treatment response of patients with cancers, acute coronary syndrome and several sepsis [21-24]. However, SIRI and PIV are not indexes previously evaluated in inflammatory ocular diseases. To the best of our knowledge, this is the first report evaluating NLR, PLR, LMR, SII, SIRI and PIV parameters in patients with cataract.

Material and Methods

Ninety-five cataract patients and 80 healthy controls who were examined at the Ophthalmology clinics of Aksaray University Education and Research Hospital between January 2022 and January 2023 were included in this retrospective study. The present study was conducted in accordance with the Helsinki Declaration rules, and informed consent forms were obtained from all the participants. The present study was approved by the Aksaray University Local Ethics Committee (protocol number: 22-SBKAEK).

Patients with systemic diseases, including systemic infection and inflammatory disease were excluded from the study. In addition, patients with previous ocular surgery, uveitis, glaucoma, pseudoexfoliation syndrome, and retinal disease were excluded. The patient group had a best-corrected visual acuity (BCVA) of 20/40 or less with the Snellen chart. In anterior segment examination with a biomicroscope, the patient group had a senile cataract grade above 3, and dilated fundus evaluation was normal. The age- and sex-matched healthy group had BCVA of better than 20/25 with the Snellen chart. In the healthy group, the anterior segment and fundus examination were normal. In addition, patient and healthy groups were classified according to the presence of diabetes mellitus (DM). Demographic information, hemogram and biochemical parameters of the study and healthy groups were collected from the hospital automation system. The hemogram parameters, low-density lipoprotein (LDL), and serum C-reactive protein (CRP) levels were assessed. Neutrophil, lymphocyte, platelet and monocyte levels of groups were used in the complete blood parameters. The NLR, PLR, LMR, SII, SIRI and PIV, respectively, were calculated as follows: the ratio of neutrophils to lymphocytes, platelets to lymphocytes, lymphocytes to monocytes, that of platelets x (neutrophils/lymphocytes), (neutrophils x monocytes)/lymphocytes and (neutrophils x platelets x monocytes)/lymphocytes.

Statistical Analysis

IBM SPSS 22 was used for the statistical analysis of the groups. The Kolmogorov-Smirnov test was used to determine whether the data were normally distributed or not. Categorical variables were expressed as numbers and percentages, and differences between groups were determined using the chi-squared test. Continuous variables were compared using Student's t-test and expressed as means ± standard deviation. Values that did not fit the normal distribution were compared using the Mann-Whitney U test. A statistically significant p-value was accepted as <0.05.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

The mean age was 68.3 ± 12.1 years, and 54.7% of cataract patients were females. In the control group, the mean age was 66.5 ± 5.4 years, and 32.5% of the participants were females. There was no statistically significant difference between the groups in terms of age and gender (Table 1).

Diabetes mellitus was present in 42% of the cataract patients and 24% of the control group. A statistically significant difference was found between the two groups in terms of DM (p=0.01). The median (min-max) outcomes of the hemogram parameters and indexes between the groups are shown in Table

Table 1. Demographic information of the study groups.

Parameter		Cataract (n=95) n %	Control (n=80) n %	P
Gender	Male	43 (45.3%)	54 (67.5%)	0.61*
	Female	52 (54.7%)	26 (32.5%)	
Age (year) mean±SD		68.3 ± 12.1	66.5 ±5.4	0.25¥
DM		40 (42.1 %)	19 (23.8 %)	0.01¥

*Chi-Square test ¥ Student's t-test; DM: Diabetes Mellitus

Table 2. Comparison of the blood parameters of the study and control groups.

Parameters	Cataract (n=95) median (min-max)	Control (n=80) median (min-max)	P*
White Blood Cell (10^3µL)	7.1 (4.1-16.1)	7.9 (4.5-13.5)	0.10
Neutrophil (10^3µL)	4.5 (2.1-9.6)	4.9 (2.3-9.5)	0.252
Lymphocyte (10^3µL)	2.4 (0.4-9.5)	2.5 (0.6-4.9)	0.814
Hemoglobin (g/dL)	13.3 (7.9-17.3)	14.5 (10.6 -17.1)	0.001
RDW (%)	14 (11.8-25.6)	13.8 (10.6 -21.4)	0.195
Platelet (10^3µL)	255 (114-489)	249 (124-417)	0.588
MPV (fl)	9.4 (7.5-12.4)	9.5 (7.3 -12.9)	0.311
LDL (mg/dL)	103 (68-183)	110 (50-252)	0.226
NLR	2.5 (0.45-12.8)	2.52 (0.84-10.5)	0.503
PLR	125 (0.59-440.5)	123.6 (63.9-450)	0.986
LMR	4.42 (1.5-54.2)	4.6 (0.86-10.3)	0.804
SII	513.6 (168.9-3101)	487.3 (226.9-3037.5)	0.431
SIRI	1.06 (0.17- 4.2)	1.28 (0.27-7.8)	0.717
PIV	248.2 (2.1-1670)	256.3 (68-2247)	0.498
CRP (mg/L)	2.48 (0.6-4.9)	1.8 (0.3-7.6)	0.07

*Mann-Whitney U test NLR: Neutrophil to Lymphocyte Ratio, PLR: Platelet to Lymphocyte ratio, LMR: Lymphocyte to Monocyte Ratio, SII: Systemic inflammatory index (neutrophil x platelet/lymphocyte count), SIRI: Systemic inflammatory response index (neutrophil × monocyte/lymphocyte count) and PIV: Pan-immune inflammation value (neutrophil × platelet x monocyte /lymphocyte count, CRP: C-reactive protein

2.

There was no significant difference between the patient and control groups in terms of laboratory parameters (p>0.05). In addition, inflammatory indices were calculated for the patient and control groups. No statistically significant difference was found between NLR, PLR, LMR, SII, SIRI, and PIV indices between the groups (p>0.05, Table 2).

Discussion

To the best of our knowledge, this is the first study to examine hemogram parameters and novel inflammatory indices including NLR, PLR, LMR, SII, SIRI, PIV together in patients with cataract. In the present study, we aimed to compare hemogram parameters and calculated novel inflammatory indices between patient and control groups. Hemogram parameters and inflammatory indices were not significantly different between the two groups.

Studies have reported that the risk of age-related cataracts increases with OI as a result of local factors or a combination of systemic inflammatory conditions [11, 13]. Klein et al. reported that markers of inflammation, including intracellular adhesion molecule-1 and IL-6, were significantly associated with age-related cataracts [11]. In another study, Chen et al. reported that inflammatory cytokines such as IL-2, and IFN-γ were significantly increased in age-related cataract and inflammatory cataract patients [13]. Erdal et al. reported that calprotectin levels were statistically significant compared to the patient and control groups in their study, in which they determined the levels of calprotectin, an inflammatory marker, in patients with cataract. They reported that NLR and PLR levels were not different in cataract patients compared to the control group. They also hypothesized that the determination of increased serum calprotectin levels can be used to assess the severity and follow-up of the disease [14].

Clinical laboratory indicators and markers of systemic inflammatory status, including NLR, PLR, LMR, and SII, have been proposed as prognostic indicators in a variety of diseases in multiple disease studies [15]. Tang et al. indicated that in the primary open angle glaucoma group, NLR, PLR and SII levels were significantly increased compared with the control group ($p < 0.001$). However, they showed that the LMR value was lower in the primary open-angle glaucoma patients with respect to controls [16].

In another study, Ozarslan et al. found that the mean NLR, PLR and SII levels were significantly higher in dry eye patients compared to the healthy group [17]. In addition, Kocamis et al. showed an association of pseudophakic cystoid macular edema with NLR, PLR and SII in eyes without risk factors after phacoemulsification surgery [25]. In a study conducted by Erbeyli et al. they reported that SII levels were significantly higher in patients with diabetic macular edema compared to patients without diabetic macular edema [18]. Consistent with other studies, it has been reported that NLR and SII values are significantly higher in patients with retinal vein occlusion and central retinal artery occlusion compared to the healthy group [19, 20].

SIRI and PIV are newly designed indexes that are considered easily calculable and comprehensive indicators of immune response and systemic inflammation. They are not previously evaluated in inflammatory ocular diseases. Han et al.'s study of 1724 patients with acute coronary syndrome reported that SIRI was significantly associated with major adverse cardiovascular conditions [24]. A meta-analysis encompassing 15 studies revealed that cancer patients with higher PIV levels had a significantly increased risk of death compared to those with lower PIV levels [23].

Conclusion

In conclusion, SII, SIRI and PIV is a new inflammatory indexes that can be used in the evaluation of patients with cataracts. Consequently, measurement of hemogram parameters and inflammatory indexes created with their combination may contribute to monitoring the progression of the cataracts.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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